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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,500	ZHANG ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/8/02&4/29/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-20 are pending. Claims 17-20 are withdrawn from consideration as drawn to non-elected inventions. Claims 1-16 are examined.

Election/Restrictions

2. Applicant's election of Group I (claims 1-16), and the species of gold solid support, peptidyl group as the presenting group, cysteine as the terminal amino acid, and oligoglycine as the central linker, in the reply filed on 9/01/2004 is acknowledged. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Upon search and further consideration, the species of silica and glass (claims 4 and 12) are rejoined.

3. Claims 17-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/01/04.

Priority

4. The instant Application, filed 2/8/2002, claims priority as a continuation application of Application No. 08/882,415, filed 6/25/1997, now US 6,368,877. Pending application 10/317,838, filed 12/11/2002, claims priority as a continuation application of the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-7 of U.S. Patent No. 6,368,877 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the composition of the claims of the instant application, comprising a solid support and a self-assembled monolayer of linear peptides bound in a pre-determined pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a cell surface protein, and a central linker, are obvious over the composition comprising a solid support and a printed pattern comprising a self-assembled monolayer of two or more different linear peptides, wherein said peptides are bound to said solid support by a bond between the solid support and a terminal amino acid, as in the claims of U.S. Patent No. 6,368,877.

6. Claims 1-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-6 of copending Application No. 10/317,838. Although the conflicting claims are not identical, they are

not patentably distinct from each other because the composition of the claims of the instant application, comprising a solid support and a self-assembled monolayer of linear peptides bound in a pre-determined pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a cell surface protein, and a central linker, are obvious over the devices comprising a solid support and an array of isolated regions on the support, the array comprising a layer of peptides, wherein the peptides are bound to the support by a bond between the support and a terminal amino acid in a reproducible pattern, and variants thereof, as in the claims of Application No. 10/317,838.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "predetermined" in claims 1 and 9, and their dependent claims, is a relative term which renders the claim indefinite. The term "predetermined" is not defined by the claims, the specification does not provide a standard for ascertaining the

requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. While the instant Specification, at p. 10, lines 15-17, defines "predetermined pattern" to mean that "the solid support has ordered areas where the peptides are bonded and not bonded to the solid support", the mental steps by which patterns are "predetermined" are not clear. Furthermore, it is unclear as how to determine whether a pattern of bonded peptide is "predetermined".

Claim 13 appears to recite an improper Markush group because it is not clear if "ligand", "a central linker between the terminal amino acid" or "presenting group" are to be included in said group.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a *Written Description Rejection.*

Claims 1-8 and 14 are drawn to compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pre-determined pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a

cell surface protein, and a central linker, and compositions comprising a solid support and a self-assembled monolayer of linear peptides bound to in a pattern to said solid support by a bond between the solid support and a terminal amino acid of linear peptides, and wherein the linear peptides comprise a presenting group is a peptidyl group which possesses an affinity to a target molecule.

The instant Specification, for example at p. 2, lines 16-24 and p. 6, line 6-p. 8, line 2, contemplate solid supports presenting peptides that bind to targets, most preferably target molecules that are present on the surfaces of cells. These target molecules include tumor markers, cellular receptors, such as CD4 and CD8, neuronal cell receptors including N-CAMs, L1 receptors, NGF receptor, netrin receptors and others. Targets can include non-cellular targets, including viruses and proteins. The specification at p. 18, lines 13-19, discloses preferred peptides include peptides wherein the presenting group is a cell adhesion motif or peptide which binds to neuronal cells; such as cell adhesion motifs that are (RADX)(SEQ ID No:2), $(RADS)_n$ (SEQ ID No:3), $(EAKX)_n$ (SEQ ID No:4), and $(EAKS)_n$ (SEQ ID No:5), wherein X is an amino acid, such as S, and n is an integer, preferably between about 2 to about 8. The specification at p. 19, lines 9-14, disclose working examples where the "RADSC" peptide was coated onto surfaces which were then capable of cell attachment.

The prior art of Prieto et al., (Proc. Natl. Acad. Sci. USA. Vol. 90, pp. 10154-10158, November 1993), at p. 10154, para 1-2, teaches that there are a plurality of different proteins and protein families with distinct domains that mediate cell adhesion. Prieto et al., at p. 10154, para 2, teach that different cell adhesion peptide motifs are not

conserved among different species, so that the RGD tripeptide, while is present in the chicken and human homologs, is absent in the mouse, newt, and pig, where it is replaced by variants. Prieto et al. at p. 10157, para 2-4, teach that mutation of cell adhesion motifs, such as RGD to RAD, are found by experimentation to completely abolish cell adhesion.

The claims are drawn to compositions comprising a solid support and pre-determined patterns of monolayers of linear peptides that bind specifically to a cell surface protein, or monolayers of linear peptides comprising a peptidyl presenting group that possesses an affinity to a target molecule. The claims do not require that the peptides possess any particular amino acid sequence, conserved structure, or other distinguishing feature. Furthermore, the specification does not describe the genus of pre-determined patterns of monolayers, and does not describe how to distinguish pre-determined monolayers of linear peptides from monolayers that are not pre-determined. Thus, the claims are drawn to a genus of peptides whose essential feature is that defined by being able to specifically bind to a cell surface protein or a target molecule.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and / or chemical properties, functional characteristics, structure / function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed in the specification are the peptides (RADX) (SEQ ID No:2), $(RADS)_n$ (SEQ ID No:3),

$(EAKX)_n$ (SEQ ID No:4), and $(EAKS)_n$ (SEQ ID No:5), wherein X is an amino acid, such as S, and n is an integer, preferably between about 2 to about 8 and the "RADSC" peptide. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure / function correlation for any cell surface protein or any target molecule. The specification does not describe pre-determined patterns of monolayers of linear peptides, such that one of skill in the would have adequate notice of what is claimed. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ 2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See Vas-Cath at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of peptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated peptides comprising the amino acid sequence set forth in the peptides (RADX) (SEQ ID No:2), $(RADS)_n$ (SEQ ID No:3), $(EAKX)_n$ (SEQ ID No:4), and $(EAKS)_n$ (SEQ ID No:5), wherein X is an amino acid, such as S, and n is an integer, preferably between about 2 to about 8 and the "RADSC" peptide, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 § 112 is severable from its enablement provision.

9. Claims 1-8 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immobilizing biological material by substrates coated with a peptide monolayer where the peptides are (RADX) (SEQ ID No:2), $(RADS)_n$ (SEQ ID No:3), $(EAKX)_n$ (SEQ ID No:4), and $(EAKS)_n$ (SEQ ID No:5), wherein X is an amino acid, such as S, and n is an integer, preferably between about 2 to about 8 and the "RADSC" peptide, does not reasonably provide enablement for immobilizing any cell surface protein or target molecule using any monolayer of linear peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether undue experiment is necessitated. These factors can include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the relative skill of those in the art;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1 and 2) The breadth of the claims and the nature of the invention: Claims 1-8 and 14 are drawn broadly to compositions comprising a solid support and pre-determined patterns of monolayers of linear peptides that bind specifically to a cell surface protein, or monolayers of linear peptides comprising a peptidyl presenting group that possesses an affinity to any target molecule.

(3 and 5) The state of the prior art and the level of predictability in the art The prior art of Prieto et al., (Proc. Natl. Acad. Sci. USA. Vol. 90, pp. 10154-10158, November 1993), at p. 10154, para 1-2 teaches that there are a plurality of different proteins and protein families with distinct domains that mediate cell adhesion. Prieto et al., at p. 10154, para 2, teach that different cell adhesion peptide motifs is not conserved among different species, so that the RGD tripeptide, while present in the chicken and human homologs, is absent in the mouse, newt, and pig, where it is

replaced by variants. Prieto et al. at p. 10157, para 2-4, teach mutation of cell adhesion motifs, such as RGD to RAD, is found by experimentation to completely abolish cell adhesion. Thus, the prior art teaches that it is unpredictable that a particular peptide motif capable of cell adhesion in one species would function similarly in another species. Furthermore, it would not be predictable that similar variants of a known cell adhesion peptide motif would also function similarly.

(4) The level of one or ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6-7) The amount of direction provided by the inventor and the existence of working examples: The instant Specification, for example at p. 2, lines 16-24 and p. 6, line 6-p. 8, line 2, contemplate solids supports presenting peptides that bind to targets, most preferably target molecules that are present on the surfaces of cells. These target molecules include tumor markers, cellular receptors, such as CD4 and CD8, neuronal cell receptors including N-CAMs, L1 receptors, NGF receptor, netrin receptors and others. Targets can include non-cellular targets, including viruses and proteins. The specification at p. 18, lines 13-19, discloses preferred peptides include peptides wherein the presenting group is a cell adhesion motif or peptide which binds to neuronal cells; such as cell adhesion motifs that are (RADX)(SEQ ID No:2), $(RADS)_n$ (SEQ ID No:3), $(EAKX)_n$ (SEQ ID No:4), and $(EAKS)_n$ (SEQ ID No:5), wherein X is an amino acid, such as S, and n is an integer, preferably between about 2 to about 8. The specification at p.

19, lines 9-14, disclose working examples where the "RADSC" peptide was coated onto surfaces which were then capable of cell attachment.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The claims contain only broad recitations of substrates comprising monolayers of linear peptides that specifically bind to cell surface molecules or to target molecules. However, the instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in carrying out the full scope of the claimed methods. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 and n.23, 20 USPQ2d 1438, 1455 and n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, undue experimentation would be required of one of ordinary skill in the art to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-5 and 9-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Mrksich et al., TibTech (Trends In Biotechnology) June 1995 (Vol. 13, no. 6), pp. 228-235.

Claims 1-5 and 9-15 are drawn to compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a cell surface protein, and a central linker between the presenting group and the terminal amino acid; and compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of linear peptides.

Mrksich et al., throughout the publication, and especially at p. 229, para 3, p. 230, para 5-p. 231, para 1, teach reproducible patterns of self-assembled monolayers (SAMs) on silicon or gold surfaces produced by microcontact printing or photolithography using a mask; at p. 231, para 3, Figure 2, teach patterned adsorption of proteins on surfaces; at p. 229, para 5-p.230, para 4, teach protein adsorption of proteins onto SAMs (taken as the bonding of an amino terminus of a polypeptide to a surface), as well as surfaces that resist adsorption of proteins, and the attachment and growth of cells on SAMs on peptides fractions of the extracellular matrix (including the peptides Arg-Gly-Asp and Tyr-Ile-Gly-Ser-Arg; at p. 232, teach SAMs as component of analytical devices; and at p. 234, Fig. 6, show a gold surface to which ethylene glycol groups and Ni(II) complexes are bound and where a histidine tagged T-cell receptor

(comprising a central linker of amino acids and a presenting group that can bind, absent evidence to the contrary, to a cell surface protein or target molecule) is bound through the histidine, *i.e.*, a terminal amino acid, to a Ni(II) complex, and thereby to the surface.

11. Claims 1, 2, 4, 6, 7, 9, 10, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Pirrung et al. (US 5,143,854) (issued 9/1/1992).

Claims 1, 2, 4, 6, 7, 9, 10, 13, and 14 are drawn to compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a cell surface protein, and a central linker between the presenting group and the terminal amino acid; and compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of linear peptides, and variations thereof.

Pirrung et al. (US 5,143,854), throughout the patent and at col. 2, lines 23-40, teach the Merrifeld method of solid phase peptide synthesis, wherein an amino acid is covalently bonded to a support made of an insoluble polymer or other material; at col. 3, lines 6-60, teach photolithography, which involve masks, to synthesize molecules at precisely known locations on a substrate; at col. 6, lines 9-21, teach monomers that can be amino acids and that can form polymers; at col. 6, lines 41-59, teach receptors that are cell membrane receptors; at col. 7, lines 49-57, teach substrates as materials having a rigid or semi-rigid surface, generally insoluble in a solvent of interest; at col. 8,

lines 1-7, teach a predefined region as a localized area on a surface that may have any convenient shape; at col. 8, lines 17-33, teach synthetic strategies and devices involving solid-phase chemistry for synthesizing peptides; at col. 8, lines 46-51, teach the optional use of linker on a surface of the substrate; at col. 9 line 14-col. 10, line 16, teach synthesizing a sequence S-L-M_a-P_1 on a region of a surface, a sequence S-L-P_0, on remaining regions of the surface (taken to read on inert, background regions), a sequence S-M_1-M_2-M3, wherein M is monomer unit, S is a surface, L is a linker molecule and P is a protecting group, and a sequence S-[L]-(M_i)-(M_j)-(M_k) . . . (M_x)-[C], wherein C is a capping unit and the square brackets indicate optional groups; at col. 10, lines 32-43, teach polymers prepared on a substrate for binding to receptors on a cell; at col. 10, lines 54-65, teach the compositions for the immobilization of cells in patterns on a surface via molecular recognition of specific polymer sequences; at col. 27, line 49-col. 29, line 68, Figure 13A-Fig. 20, teach an arrays of peptides in various patterns, including checkerboards and strips on glass slides, wherein regions comprising peptides have surrounding regions without peptides, and provide examples of array devices with a pattern.

Pirrung et al. teach photolithography and mask technology for their solid phase synthesis of attached peptides, which is inherently a self-assembled monolayer, as evidenced by Mrksich et al., TibTech June 1995 (Vol. 13), pp. 228-235. It is noted that the instant specification does not disclose any particular molecular structure that distinguishes a peptide array formed as a self-assembled monolayer from a peptide array formed by any different processes. The specification states that the composition

of matter comprises a solid support and a self-assembled monolayer of linear peptides wherein said peptides bound directly to said solid support through a terminal amino acid in a pattern. (The instant Specification at p. 2, lines 25-27). Therefore, absent evidence to the contrary, the peptide arrays of the devices taught by Pirrung et al. do not differ from the self-assembled monolayers of the claimed invention.

12. Claims 1, 4-7, 9, and 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Holmes (US 5,527,681) (issued 6/18/1996).

Claims 1, 4-7, 9, and 12-16 are drawn to compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a cell surface protein, and a central linker between the presenting group and the terminal amino acid; and compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of linear peptides, and variations thereof.

Holmes (US 5,527,681), throughout the patent and at col. 1, lines 36-45, teaches the Merrifeld method of solid phase peptide synthesis, wherein an amino acid is covalently bonded to a support made of an insoluble polymer or other material; at col. 2, lines 1-43, teach photolithography, which involve masks, to synthesize molecules at precisely known locations on a substrate; at col. 4, lines 43-61, teach receptors that include cell surface receptor molecules; at col. 4, line 66-col. 5, line 28, teaches

substrates as materials having a rigid or semi-rigid surface, generally insoluble in a solvent of interest, and a predefined region as a localized area on a surface; at col. 6, lines 56-67, teaches synthetic strategies and devices involving solid-phase chemistry for synthesizing peptides; at col. 7, lines 31-35, teaches the optional use of linker on a surface of the substrate; at col. 7, lines 43-48, teach glass substrates; at col. 8, line 5-col. 9, line 20, teaches synthesizing a sequence S-L-M_1-P on a region of a surface, as well as remaining regions of the surface (taken to read on inert, background regions), a sequence S-L-P_σ, a sequence S-M_1-M_2-M3, wherein M is monomer unit, S is a surface, L is a linker molecule and P is a protecting group, and a sequence S-[L]-(M_i)-(M_j)-(M_k) . . . (M_x)-[C], wherein C is a capping unit and the square brackets indicate optional groups; at col. 9, lines 22-34, teach polymers prepared on the substrate that may be used for receptors on a cell; at col. 9, lines 50-55, teaches the compositions for the immobilization of cells in patterns on a surface via molecular recognition of specific polymer sequences; at col. 10, line 66-col. 11, line 26, teaches an array of peptides; at col. 14, line 57-col. 15, line 7, teach a tether molecule (T) coupled to a surface of the substrate, where T may be a monomer in a polymer, such as glutamic acid, serine, cysteine; at col. 17, lines 28-39, teaches monomers, such as glutamic acid, that are readily attachable to the substrate; and at col. 26, lines 20-40, teach the application of photolithography to create arrays of spatially-addressable chemical libraries, and provide examples of pairs of slides comprising the same polypeptide, indicating the manufacture of devices with a pattern.

Holmes teaches photolithography and mask technology for their solid phase synthesis of the attached peptides, which is inherently a self-assembled monolayer, as evidenced by Mrksich et al., TibTech June 1995 (Vol. 13), pp. 228-235. It is noted that the instant specification does not disclose any particular molecular structure that distinguish a peptide array formed as a self-assembled monolayer from a peptide array formed by different processes. Therefore, absent evidence to the contrary, the peptide arrays of the devices taught by Holmes do not differ from the self-assembled monolayers of the claimed invention.

13. Claims 1, 9, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Kauvar (US 5,384,263) (issued 1/24/1995).

Kauvar (US 5,384,263), at col. 21, line 65-col. 22, line 16, teach antibodies that target tumor cell surface antigens; at col. 23, line 66-col. 24, line 46, teaches a reproducible array pattern of antibodies that are bound to an activated membrane, which absent evidence to the contrary, comprises antibodies having a bond between the substrate and a terminal amino acid residue, in some fraction of the total number of bound antibodies.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1 and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of **Mrksich et al.**, TibTech (Trends In Biotechnology) June 1995 (Vol. 13, no. 6), pp. 228-235; **Pirrung et al.** (US 5,143,854); or **Holmes**, (US 5,527,681), each taken separately; and further in view of **Schatz et al.**, (US 5,270,170).

Claims 1 and 5-8 are drawn to compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of the linear peptides, said peptides comprising a presenting group that binds specifically to a cell surface protein, and a central linker between the presenting group and the terminal amino acid; and compositions comprising a solid support and a self-assembled monolayer of linear peptides bound in a pattern to said solid support by a bond between the solid support and a terminal amino acid of linear peptides, and wherein the central linker comprises between 2 to 50 amino acids (claim 7) and wherein the central linker is oligoglycine or oligoalanine (claim 8).

Mrksich et al., throughout the publication, and especially at p. 229, para 3, p. 230, para 5-p. 231, para 1, teach reproducible patterns of self-assembled monolayers (SAMs) on silicon or gold surfaces produced by microcontact printing or

photolithography using a mask; at p. 231, para 3, Figure 2, teach patterned adsorption of proteins on surfaces; at p. 229, para 5-p.230, para 4, teach protein adsorption of proteins onto SAMs (taken as the bonding of an amino terminus of a polypeptide to a surface), as well as surfaces that resist adsorption of proteins, and the attachment and growth of cells on SAMs on peptides fractions of the extracellular matrix (including the peptides Arg-Gly-Asp and Tyr-Ile-Gly-Ser-Arg; at p. 232, teach SAMs as component of analytical devices; and at p. 234, Fig. 6, show a gold surface to which ethylene glycol groups and Ni(II) complexes are bound and where a histidine tagged T-cell receptor (comprising a central linker of amino acids and a presenting group that can bind, absent evidence to the contrary, to a cell surface protein or target molecule) is bound through the histidine, *i.e.*, a terminal amino acid, to a Ni(II) complex, and thereby to the surface.

Pirrung et al., (US 5,143,854), throughout the patent and at col. 2, lines 23-40, teach the Merrifeld method of solid phase peptide synthesis, wherein an amino acid is covalently bonded to a support made of an insoluble polymer or other material; at col. 3, lines 6-60, teach photolithography, which involve masks, to synthesize molecules at precisely known locations on a substrate; at col. 6, lines 9-21, teach monomers that can be amino acids and that can form polymers; at col. 6, lines 41-59, teach receptors that are cell membrane receptors; at col. 7, lines 49-57, teach substrates as materials having a rigid or semi-rigid surface, generally insoluble in a solvent of interest; at col. 8, lines 1-7, teach a predefined region as a localized area on a surface that may have any convenient shape; at col. 8, lines 17-33, teach synthetic strategies and devices involving solid-phase chemistry for synthesizing peptides; at col. 8, lines 46-51, teach the optional

use of linker on a surface of the substrate; at col. 9 line 14-col. 10, line 16, teach synthesizing a sequence S-L-M_a-P_1 on a region of a surface, a sequence S-L-P_0, on remaining regions of the surface (taken to read on inert, background regions), a sequence S-M_1-M_2-M3, wherein M is monomer unit, S is a surface, L is a linker molecule and P is a protecting group, and a sequence S-[L]-(M_i)-(M_j)-(M_k) . . . (M_x)-[C], wherein C is a capping unit and the square brackets indicate optional groups; at col. 10, lines 32-43, teach polymers prepared on a substrate for binding to receptors on a cell; at col. 10, lines 54-65, teach the compositions for the immobilization of cells in patterns on a surface via molecular recognition of specific polymer sequences; at col. 27, line 49-col. 29, line 68, Figure 13A-Fig. 20, teach an arrays of peptides in various patterns, including checkerboards and strips on glass slides, wherein regions comprising peptides have surrounding regions without peptides, and provide examples of array devices with a preselected, reproducible pattern.

Holmes, (US 5,527,681), throughout the patent and at col. 1, lines 36-45, teaches the Merrifeld method of solid phase peptide synthesis, wherein an amino acid is covalently bonded to a support made of an insoluble polymer or other material; at col. 2, lines 1-43, teach photolithography, which involve masks, to synthesize molecules at precisely known locations on a substrate; at col. 4, lines 43-61, teach receptors that include cell surface receptor molecules; at col. 4, line 66-col. 5, line 28, teaches substrates as materials having a rigid or semi-rigid surface, generally insoluble in a solvent of interest, and a predefined region as a localized area on a surface; at col. 6, lines 56-67, teaches synthetic strategies and devices involving solid-phase chemistry for

synthesizing peptides; at col. 7, lines 31-35, teaches the optional use of linker on a surface of the substrate; at col. 7, lines 43-48, teach glass substrates; at col. 8, line 5-col. 9, line 20, teaches synthesizing a sequence S-L-M_1-P on a region of a surface, as well as remaining regions of the surface (taken to read on inert, background regions), a sequence S-L-P_σ, a sequence S-M_1-M_2-M3, wherein M is monomer unit, S is a surface, L is a linker molecule and P is a protecting group, and a sequence S-[L]-(M_i)-(M_j)-(M_k) . . . (M_x)-[C], wherein C is a capping unit and the square brackets indicate optional groups; at col. 9, lines 22-34, teach polymers prepared on the substrate that may be used for receptors on a cell; at col. 9, lines 50-55, teaches the compositions for the immobilization of cells in patterns on a surface via molecular recognition of specific polymer sequences; at col. 10, line 66-col. 11, line 26, teaches an array of peptides; at col. 14, line 57-col. 15, line 7, teach a tether molecule (T) coupled to a surface of the substrate, where T may be a monomer in a polymer, such as glutamic acid, serine, cysteine; at col. 17, lines 28-39, teaches monomers, such as glutamic acid, that are readily attachable to the substrate; and at col. 26, lines 20-40, teach the application of photolithography to create arrays of spatially-addressable chemical libraries, and provide examples of pairs of slides comprising the same polypeptide, indicating the manufacture of devices with a preselected, reproducible pattern.

Pirrung et al. and Holmes teaches photolithography and mask technology for their solid phase synthesis of the attached peptides, which is inherently a self-assembled monolayer, as evidenced by Mrksich et al., TibTech June 1995 (Vol. 13), pp. 228-235. It is noted that the instant specification does not disclose any particular

molecular structure that distinguish a peptide array formed as a self-assembled monolayer from a peptide array formed by different processes. Therefore, absent evidence to the contrary, the peptide arrays of the devices taught by Holmes do not differ from the self-assembled monolayers of the claimed invention.

None of the aforementioned references of Pirrung et al., Holmes or Mrksich et al., teach compositions comprising a central linker between the presenting group and the terminal amino acid wherein the central linker comprises between 2 to 50 amino acids (as in claim 7) and wherein the central linker is oligoglycine or oligoalanine (as in claim 8).

Schatz et al., (US 5,270,170), throughout the patent and especially at col. 4, lines 6-12, teach linkers or spacers that are molecules or groups of molecules that connect two molecules, such as a protein and a random peptide, and that serve to place the two molecules in a preferred configuration, e.g., so that the random peptide can bind to a receptor with minimal steric hindrance from the protein; at col. 16, lines 5-10, teach spacer molecules with 20-30 residues, and where the spacer residues are preferably at least two to three or more but usually less than eight to ten; and at col. 16, lines 19-58, spacers residues that are somewhat flexible, comprising oligoglycine, such that interaction of random peptides with selected receptors may be facilitated.

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the art to have made and used compositions comprising a central linker between the presenting group and the terminal amino acid and wherein the

central linker comprises between 2 to 50 amino acids and wherein the central linker is oligoglycine or oligoalanine, as taught by Schatz et al.

One of ordinary skill in the art would have been motivated to make and use compositions comprising a central linker between the presenting group and the terminal amino acid and wherein the central linker comprises between 2 to 50 amino acids and wherein the central linker is oligoglycine or oligoalanine, because Schatz et al. teach that liners or spacers that are oligoglycine are somewhat flexible and can be used to position peptides, which are linked to a different molecule, for binding to receptors and because Schatz et al. teach the preferable use of spacers with residues of at least two to three or more but usually less than eight to ten residues.

Conclusion

15. Claims 1-16 are rejected.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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